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Original Research Article

The Efficacy of Ketamine Gargle in Attenuating Postoperative Sore Throat: A Randomized Control Trial

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ABSTRACT:

Introduction: Postoperative sore throat (POST) is a common complication of general anesthesia with endotracheal intubation that affects the patient satisfaction after surgery. The aim of the study was to compare the effectiveness of ketamine gargle with placebo in preventing POST after endotracheal intubation. **Methods**: Sixty eight patients scheduled for elective surgery under general anesthesia were enrolled in this study. Patients were randomly allocated into two groups, 33 in study group and 35 in control group. Study group patients were asked to gargle with ketamine (50 mg in 1 ml mixed with 29 ml of drinking water) 10 minutes before induction for 30 seconds. Controls were made to do so with 30 ml of drinking water. POST was graded at one, two, four, and 24 hrs after operation on a four-point scale (0-3). The outcome measures were compared between two groups in terms of occurrence of POST and severity of POST at one, two, four, and 24 hr to determine the efficacy of ketamine. **Results**: Occurrence of POST was significantly less in study group at four hours. Severity of POST was significantly low in study group at one, two and four hours as compared to that in controls. It was comparable at 24 hours. **Conclusion**: Ketamine gargle significantly reduced the occurrence and severity of POST.

Keywords: endotracheal • intubation • ketamine • pharyngitis • postoperative

INTRODUCTION:

Postoperative sore throat (POST) is rated by patients as the eighth most undesirable outcome in the postoperative period.[1] The occurrence of POST varies from 6.6% to 90%.[2] The occurrence is highest with tracheal tube (45.4%) followed by patients with laryngeal mask airway (17.5%), while patients with facemask have lowest occurrence of sore throat (3.3%).[3] The main mechanism of POST is postulated to be irritation and inflammation of the airway.[4] POST might be a consequence of localized trauma to the pharyngeal and tracheal mucosa during laryngoscopy, intubation and endotracheal tube cuff inflation.[5]

Various measures have been used for attenuating POST with variable success. Among pharmacological methods in use are beclomethasone inhalation, gargling with aspirin and benzydamine, gargling with azulene sulfonate, local spray with lidocaine and intracuff administration of alkalized lignocaine, topical methylprednisolone, diclofenac epolamine patch, transdermal ketoprofen, and application of triamcinolone acetonide paste.[6-13] All these techniques have their own limitations and variable success rate.

Ketamine, an N-methyl-D-aspartate (NMDA) receptor antagonist, is proved to be present also in peripheral nervous system.[14,15] Peripherally administered NMDA receptor antagonists are involved with antinociception and anti-inflammatory cascade.[16,17] Various studies have been done on ketamine gargling for attenuating postoperative sore throat in other parts of world and all of them have shown reduction in occurrence and severity of POST.[18-21]

This study was done to compare the occurrence and severity of POST in two groups of

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patients, one receiving ketamine and other receiving Normal Saline for preoperative gargle.

METHODS:

This is a hospital based prospective, randomized, placebo-controlled, double-blind study conducted at National Academy of Medical Sciences, Bir Hospital for the period of three months (Nov 2012 – Jan 2013) after the approval by Hospital's Institutional Review Committee.

Based on previous similar study done by Rudra et. al,[18] we presumed the occurrence of POST to be 60% (p1), and would reduce the occurrence to 20% (p2). Power analysis with $\alpha = 0.05$, $\beta = 0.90$, p1 = 0.6 and p2 = 0.2 calculates the minimum required sample size in each group to be 33. A list of computer generated random numbers was created. A total of 68 patients were thus randomized into two groups, the first (study group) containing 33 and the second (control group) containing 35 subjects.

Patients undergoing elective surgery in Bir Hospital under general anesthesia with endotracheal intubation were enrolled in the study. Inclusion criteria were male or female of ASA I or II of age between 18 to 60 years with weight >40 kg and duration of surgery being less than 120 min. Exclusion criteria were patients' refusal and uncooperative patients, anticipated difficult airway, history of preoperative sore throat and asthma, patients of known allergy to the study drug, history of recent anti-inflammatory medication, patients with upper respiratory tract infection, patient requiring more than one attempt for passage of tracheal tube, extubation provoked bucking and patients undergoing Nose and Throat surgeries.

Pre-anesthetic checkup was done a day before surgery. Informed and written consent were taken from the patients who were enrolled in the study. Patients were informed about their right to withdraw from the study at any time. They were informed that there would be no financial burden to them since the drugs under study would be provided free. The patients who were enrolled in the study were kept nil per oral for eight hours before surgery. On the day of operation, when the patient came to operation theater, intravenous access was secured with 18 G cannula on non-dominant forearm. Patients were allocated into either of two groups according to the list of random numbers generated earlier. Anesthetic assistant provided the control group with drinking water (30 ml) and the study group with one ml (50 mg) of preservative free ketamine mixed in 29 ml of drinking water. Patients were asked to gargle with the given preparation for 30 seconds. Anesthesia was induced 10 minutes later. Investigator was blinded to the study drug used.

Monitors were attached which include continuous electrocardiogram, non-invasive blood pressure, pulse oximetry. Then injection pethidine 0.75 mg/kg was given for analgesia. After preoxygenation with five breaths of 100% oxygen, induction agent propofol was given and titrated till the eye lash reflex get obtunded. The patients were ventilated with tight fitted mask with oxygen. Once the possibility of ventilation was confirmed, muscle relaxant vecuronium 0.12 mg/kg was given, then ventilated with oxygen and one percent halothane for three min. Then patients were intubated with sterile polyvinyl chloride endotracheal tube (high volume low pressure cuffs) with an internal diameter of seven mm for women and 7.5 mm for men. The tracheal intubation was performed by experienced anesthesiologist. Immediately after intubation, cuff of the endotracheal tube was filled with a volume of room air required to prevent an audible air leak. Anesthesia was maintained with oxygen, halothane and vecuronium. At the end of the surgery, halothane was stopped, the patients were reversed with neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg after assessing the presence of adequate volume of spontaneous respiration. Gentle suctioning of oral cavity was done and extubated when patients were awake. Patient was shifted to post-operative ward. The patients were interviewed in a standard fashion by a blinded investigator on arrival in the post anesthesia care unit when patient was able to respond (one hr), and at two, four and 24 hours using four-point POST scores (Table 1).

Occurrence and severity of post-operative sore throat was assessed in post-operative care unit at one hr, two hr, four hr, and 24 hr. Side effects

Table 1. *Postoperative Sore Throat (POST) scores*

POST score	Definition
0	No Sore Throat
1	Mild Sore Throat (complain of sore throat only on asking)
2	Moderate Sore Throat (complain of sore throat on his/her own)
3	Severe Sore Throat (change of voice or hoarseness associated with throat pain)

like hallucination, nausea, vomiting, vertigo, and nystagmus were looked for at one hr of extubation in postoperative care unit.

Data were collected in Microsoft Excel 2007 and analyzed by statistical software-SPSS 16. Appropriate tests like T-test for difference of mean, Chi-square test for categorical data and Wilcoxon rank sum test for ordinal data were used. $P<0.05$ was considered statistically significant.

RESULTS:

A total of 68 patients were included in the study. There were 33 in study group and 35 in control group. There was no difference among the two groups with regard to ASA status, age, gender, weight, duration of surgery, duration of anesthesia (Table 2).

Occurrence of sore throat was significantly less in ketamine group at four hr post extubation. Though not significant, occurrence was lower in ketamine group at all other times (Table 3). The severity of sore throat was significantly less in ketamine group at four hr post extubation (Table 4). No local or systemic side effects were observed.

Table 2: Patient characteristics

Variables	Study Group	Controls	Statistics
Number (*n*)	33	35	
Gender: M	11	8	X^2=1.72, *df*=1
F	22	27	*p*=0.19
Age (years) *M (SD)*	39.09 (14.68)	39.97 (12.4)	*t*=-0.27, *df*=66, *p*=0.79
Weight (kg) *M (SD)*	54.71 (9.83)	57.21 (8.92)	*t*= -1.1, *df*=66, *p*=0.28
ASA: I	27	24	X^2=1.59, *df*=1
II	6	11	*p*=0.21
Duration of surgery in min, *M (SD)*	64.84 (25.54)	59.53 (26.35)	*t*=0.84, *df*=66, *p*=0.4
Duration of anesthesia in min, *M (SD)*	86.06 (26.03)	82.03 (30.02)	*t*=0.59, *df*=66, *p*=0.56

Table 3: Occurrence of sore throat at 1, 2, 4 and 24 hour post extubation

Occurrence of POST (hr after extubation)	Study group (*n*=33)	Controls (*n*=35)	*p*
1 hr, *n (SD)*	5 (15.1%)	12 (34.3%)	X^2=2.88 *p*=0.09
2 hr, *n (SD)*	9 (27%)	18 (51.4%)	X^2=3 *p*=0.08
4 hr, *n (SD)*	4 (12.1%)	15 (42.9%)	X^2=6.37 ***p*=0.01**
24 hr, *n (SD)*	2 (6%)	8 (22.9%)	X^2=3.6 *p*=0.06

DISCUSSION:

Several factors have been attributed to the occurrence of postoperative sore throat like gender, age, size of endotracheal tube, grade of difficulty of intubation, duration of surgery.[22,23] In our study, two study groups were not statistically different in terms of gender, age, weight, duration of surgery and duration of intubation.

In recent years, studies have shown that ketamine has its anti-inflammatory properties and it plays a protective role against lung injury.[4] The effect of nebulized ketamine inhalation on allergen-induced rats have been examined in the study done by Zhu et al. and they concluded that ketamine administration by local route appears to inhibit the inflammatory cascade response.[17] Besides, experimental studies point out that peripherally administered NMDA receptor antagonists are implicated with antinociception.[24]

In our study, the maximum occurrence of POST was 51.4% at two hrs in Controls. Occurrence of POST was reduced significantly at four hours in study group compared to Controls. It was comparable between two groups at one, two and 24 hours. This reduction in occurrence and severity of POST is consistent with the findings of previous studies.[18-21]

The severity of pain was statistically less in study group at one, two and four hours as compared to controls. However, pain at 24 hours was not significantly different.

There are some limitations of our study. We did not measure the plasma level of ketamine. So we cannot rule out the role of systemic effect of ketamine in our results. We had powered our study to the occurrence of sore throat. The power of this study may not be sufficient for the severity of those events.

CONCLUSION:

In conclusion, ketamine gargle before induction in patients undergoing general anesthesia with endotracheal intubation is effective and safe in reducing the occurrence and severity of postoperative sore throat. It significantly reduces the occurrence and severity of POST at four hrs post extubation.

Conflict of interest declared: None

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